

Human Perivascular Stem Cell-Based Bone Graft Substitute Induces Rat Spinal Fusion.

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Funding Grants: Harnessing native fat-residing stem cells for bone regeneration

Public Summary:

We have previously identified a novel class of multi-lineage human stem cells that are adherent to blood vessels throughout the organism, at all ages of life. These cells, named perivascular stem cells (PSC) have been validated preclinically and are most promising to treat multiple human conditions, notably in orthopaedic medicine. Here we have tested in rats the ability of human PSC extracted from adipose tissue to mediate spine fusion, a procedure in which two vertebrae are fused, in indications of untreatable severe back pain, severe scoliosis... We show in this model that PSC rapidly and efficiently induce osteogenesis and spine fusion, generating new bone tissue that is structurally and mechanically normal. Some PSC differentiated directly into bone, whereas other contributed indirectly by secreting growth factors recruiting regenerative cells from the host. In summary PSC appear as easily harvested, abundant, safe and reliable regenerative cells able to produce large amounts of competent bone tissue and therefore to mediate spinal fusion.

Scientific Abstract:

Adipose tissue is an attractive source of mesenchymal stem cells (MSCs) because of its abundance and accessibility. We have previously defined a population of native MSCs termed perivascular stem cells (PSCs), purified from diverse human tissues, including adipose tissue. Human PSCs (hPSCs) are a bipartite cell population composed of pericytes (CD146⁺CD34⁺CD45⁻) and adventitial cells (CD146⁻CD34⁺CD45⁻), isolated by fluorescence-activated cell sorting and with properties identical to those of culture identified MSCs. Our previous studies showed that hPSCs exhibit improved bone formation compared with a sample-matched unpurified population (termed stromal vascular fraction); however, it is not known whether hPSCs would be efficacious in a spinal fusion model. To investigate, we evaluated the osteogenic potential of freshly sorted hPSCs without culture expansion and differentiation in a rat model of posterolateral lumbar spinal fusion. We compared increasing dosages of implanted hPSCs to assess for dose-dependent efficacy. All hPSC treatment groups induced successful spinal fusion, assessed by manual palpation and microcomputed tomography. Computerized biomechanical simulation (finite element analysis) further demonstrated bone fusion with hPSC treatment. Histological analyses showed robust endochondral ossification in hPSC-treated samples. Finally, we confirmed that implanted hPSCs indeed differentiated into osteoblasts and osteocytes; however, the majority of the new bone formation was of host origin. These results suggest that implanted hPSCs positively regulate bone formation via direct and paracrine mechanisms. In summary, hPSCs are a readily available MSC population that effectively forms bone without requirements for culture or predifferentiation. Thus, hPSC-based products show promise for future efforts in clinical bone regeneration and repair.

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